CLAIMS

What is claimed is:

1. A method of diagnosing a susceptibility to myocardial infarction or stroke in an individual, comprising detecting a polymorphism in a FLAP nucleic acid, wherein the presence of the polymorphism in the nucleic acid is indicative of a susceptibility to myocardial infarction or stroke.

2. A method of diagnosing a susceptibility to myocardial infarction or stroke, comprising detecting an alteration in the expression or composition of a polypeptide encoded by a FLAP nucleic acid in a test sample, in comparison with the expression or composition of a polypeptide encoded by a FLAP nucleic acid in a control sample, wherein the presence of an alteration in expression or composition of the polypeptide in the test sample is indicative of a susceptibility to myocardial infarction or stroke.

3. The method of Claim 1 wherein the polymorphism in the FLAP nucleic acid is indicated by detecting the presence of a haplotype comprising one or more of the markers DG00AAFIU, SG13S25, DG00AAJFF, DG00AAHII, DG00AAHID, B_SNP_310657, SG13S30, SG13S32, SG13S42, and SG13S35 at the 13q12 locus comprising a FLAP nucleic acid.

4. The method of Claim 1 wherein the polymorphism comprises at least one of the polymorphisms as indicated in Table 3.

5. An isolated nucleic acid molecule comprising a FLAP nucleic acid, wherein the FLAP nucleic acid has a nucleic acid sequence of SEQ ID NO: 1 or SEQ ID NO: 3, or the complement of SEQ ID NO: 1 or SEQ ID NO: 3, wherein the nucleic acid molecule comprises a polymorphism as indicated in Table 3.

6. An isolated nucleic acid molecule having a polymorphism as indicated in Table 3, which hybridizes under high stringency conditions to a nucleic acid sequence of SEQ ID NO: 1 or SEQ ID NO: 3, or the complement of SEQ ID NO: 1 or SEQ ID NO: 3.

7. A method for assaying for the presence of a first nucleic acid molecule in a sample, comprising contacting said sample with a second nucleic acid molecule, where the second nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 1 or SEQ ID NO: 3, and hybridizes to the first nucleic acid under high stringency conditions.

8. A vector comprising an isolated nucleic acid molecule selected from the group consisting of:

a) a nucleic acid sequence of SEQ ID NO: 1 or SEQ ID NO: 3; or

b) complement of a nucleic acid sequence of SEQ ID NO: 1 or SEQ ID NO: 3;

wherein the nucleic acid molecule is operably linked to a regulatory sequence.

9. A recombinant host cell comprising the vector of Claim 8.

10. A method for producing a polypeptide encoded by an isolated nucleic acid molecule having a polymorphism as indicated in Table 3, comprising culturing the recombinant host cell of Claim 9 under conditions suitable for expression of the nucleic acid molecule.

11. A method of assaying for the presence of a polypeptide encoded by an isolated nucleic acid molecule according to Claim 5 in a sample, the method comprising contacting the sample with an antibody which specifically binds to the encoded polypeptide.

12. A method of identifying an agent that alters expression of a FLAP nucleic acid, comprising:

a) contacting a solution containing a nucleic acid comprising the promoter region of the FLAP nucleic acid operably linked to a reporter gene with an agent to be tested;

b) assessing the level of expression of the reporter gene; and

c) comparing the level of expression with a level of expression of the reporter gene in the absence of the agent; wherein if the level of expression of the reporter gene in the presence of the agent differs, by an amount that is statistically significant, from the level of expression in the absence of the agent, then the agent is an agent that alters expression of the FLAP nucleic acid.

13. An agent that alters expression of the FLAP nucleic acid, identifiable according to the method of Claim 12.

14. A method of identifying an agent that alters expression of a FLAP nucleic acid, comprising:

a) contacting a solution containing a nucleic acid of Claim 5 or a derivative or fragment thereof with an agent to be tested;

b) comparing expression with expression of the nucleic acid, derivative or fragment in the absence of the agent;

wherein if expression of the nucleotide, derivative or fragment in the presence of the agent differs, by an amount that is statistically significant, from the expression in the absence of the agent, then the agent is an agent that alters expression of the FLAP nucleic acid.

15. The method of Claim 14, wherein the expression of the nucleotide, derivative or fragment in the presence of the agent comprises expression of one or more splicing variant(s) that differ in kind or in quantity from the expression of one or more splicing variant(s) the absence of the agent.

16. An agent that alters expression of a FLAP nucleic acid, identifiable according to the method of Claim 14.

17. An agent that alters expression of a FLAP nucleic acid, selected from the group consisting of: antisense nucleic acid to a FLAP nucleic acid; a FLAP polypeptide; a FLAP nucleic acid receptor; a FLAP nucleic acid binding agent; a peptidomimetic; a fusion protein; a prodrug thereof; an antibody; and a ribozyme.

18. A method of altering expression of a FLAP nucleic acid, comprising contacting a cell containing a FLAP nucleic acid with an agent of Claim 17.

19. A method of identifying a polypeptide which interacts with a FLAP polypeptide, comprising employing a yeast two-hybrid system using a first vector which comprises a nucleic acid encoding a DNA binding domain and a FLAP polypeptide, splicing variant, or a fragment or derivative thereof, and a second vector which comprises a nucleic acid encoding a transcription activation domain and a nucleic acid encoding a test polypeptide, wherein if transcriptional activation occurs in the yeast two-hybrid system, the test polypeptide is a polypeptide which interacts with a FLAP polypeptide.

20. A transgenic animal comprising a nucleic acid selected from the group consisting of: an exogenous FLAP nucleic acid and a nucleic acid encoding a FLAP polypeptide.

21. A method for assaying a sample for the presence of a FLAP nucleic acid, comprising:

a) contacting said sample with a nucleic acid comprising a contiguous nucleic acid sequence which is at least partially complementary to a part

of the sequence of said FLAP nucleic acid under conditions appropriate for hybridization; and

b) assessing whether hybridization has occurred between a FLAP nucleic acid nucleic acid and said nucleic acid comprising a contiguous nucleotide sequence which is at least partially complementary to a part of the sequence of said FLAP nucleic acid;

wherein if hybridization has occurred, a FLAP nucleic acid is present in the nucleic acid.

22. The method of Claim 21, wherein said nucleic acid comprising a contiguous nucleic acid sequence is completely complementary to a part of the sequence of said FLAP nucleic acid.

23. The method of Claim 21, comprising amplification of at least part of said FLAP nucleic acid.

24. The method of Claim 21, wherein said contiguous nucleic acid sequence is 100 or fewer nucleotides in length and is either: a) at least 80% identical to a contiguous sequence of nucleotides of SEQ ID NO: 1 or SEQ ID NO: 3; b) at least 80% identical to the complement of a contiguous sequence of nucleotides of SEQ ID NO: 1 or SEQ ID NO: 3; or c) capable of selectively hybridizing to said FLAP nucleic acid.

25. A reagent for assaying a sample for the presence of a FLAP nucleic acid, said reagent comprising a nucleic acid comprising a contiguous nucleic acid sequence which is at least partially complementary to a part of the nucleic acid sequence of said nucleic acid.

26. The reagent of Claim 25, wherein the nucleic acid comprises a contiguous nucleotide sequence, which is completely complementary to a part of the nucleic acid sequence of said FLAP nucleic acid.

27. A reagent kit for assaying a sample for the presence of a FLAP nucleic acid, comprising in separate containers:

a) one or more labeled nucleic acids comprising a contiguous nucleotide sequence which is at least partially complementary to a part of the nucleic acid sequence of said FLAP nucleic acid; and

b) reagents for detection of said label.

28. The reagent kit of Claim 27, wherein the labeled nucleic acid comprises a contiguous nucleotide sequences which is completely complementary to a part of the nucleic acid sequence of said FLAP nucleic acid.

29. A reagent kit for assaying a sample for the presence of a FLAP nucleic acid, comprising one or more nucleic acids comprising a contiguous nucleic acid sequence which is at least partially complementary to a part of the nucleic acid sequence of said FLAP nucleic acid, and which is capable of acting as a primer for said FLAP nucleic acid when maintained under conditions for primer extension.

30. The use of a nucleic acid which is 100 or fewer nucleotides in length and which is either: a) at least 80% identical to a contiguous sequence of nucleotides of SEQ ID NO: 1 or SEQ ID NO: 3; b) at least 80% identical to

the complement of a contiguous sequence of nucleotides of SEQ ID NO: 1 or SEQ ID NO: 3; or c) capable of selectively hybridizing to said FLAP nucleic acid, for assaying a sample for the presence of a FLAP nucleic acid.

31. The use of a first nucleic acid which is 100 or fewer nucleotides in length and which is either:

a) at least 80% identical to a contiguous sequence of nucleotides of SEQ ID NO: 1 or SEQ ID NO: 3;

b) at least 80% identical to the complement of a contiguous sequence of nucleotides of SEQ ID NO: 1 or SEQ ID NO: 3; or

c) capable of selectively hybridizing to said FLAP nucleic acid; for assaying a sample for the presence of a FLAP nucleic acid that has at least one nucleotide difference from the first nucleic acid.

32. The use of a nucleic acid which is 100 or fewer nucleotides in length and which is either:

a) at least 80% identical to a contiguous sequence of nucleotides in one of the nucleic acid sequences as shown in Table 3;

b) at least 80% identical to the complement of a contiguous sequence of nucleotides in one of the nucleic acid sequences as shown in Table 3; or

c) capable of selectively hybridizing to said FLAP nucleic acid;

for diagnosing a susceptibility to a disease or condition associated with a FLAP nucleic acid.

33. A method of diagnosing a susceptibility to myocardial infarction or stroke in an individual, comprising determining the presence or absence in the individual of a haplotype using one or more of the markers DG00AAFIU, SG13S25, DG00AAJFF, DG00AAHII, DG00AAHID, B_SNP_310657, SG13S30, SG13S32, SG13S42, and SG13S35, with alleles T, G, G, G, T, G, G, A, A and G at the 13q12 loci comprising a FLAP nucleic acid, wherein the

presence of the haplotype is diagnostic of susceptibility to myocardial infarction or stroke.

34. The method of Claim 33, wherein determining the presence or absence of the haplotype comprises enzymatic amplification of nucleic acid from the individual.

35. The method of claim 34, wherein determining the presence or absence of the haplotype further comprises electrophoretic analysis.

36. The method of claim 33, wherein determining the presence or absence of the haplotype further comprises restriction fragment length polymorphism analysis.

37. The method of claim 33, wherein determining the presence or absence of the haplotype further comprises sequence analysis.

38. A method of diagnosing a susceptibility to myocardial infarction or stroke in an individual, comprising:
obtaining a nucleic acid sample from said individual; and
analyzing the nucleic acid sample for the presence or absence of a haplotype using one or more of the markers DG00AAFIU, SG13S25, DG00AAJFF, DG00AAHII, DG00AAHID, B_SNP_310657, SG13S30, SG13S32, SG13S42, and SG13S35, with alleles T, G, G, G, T, G, G, A, A and G at the 13q12 loci comprising a FLAP nucleic acid, wherein the presence of the haplotype is diagnostic for a susceptibility to myocardial infarction or stroke.

39. A method of diagnosing a susceptibility to myocardial infarction or stroke in an individual, comprising determining the presence or absence in the individual of a haplotype comprising one or more markers and/or single nucleotide polymorphisms as shown in Table 3 in the locus on chromosome

13q12 comprising a FLAP nucleic acid, wherein the presence of the haplotype is diagnostic of a susceptibility to myocardial infarction or stroke.

40. A method of diagnosing a susceptibility to myocardial infarction or stroke in an individual, comprising determining the presence or absence in the individual of a haplotype comprising one or more markers and/or single nucleotide polymorphisms as shown in Table 13 in the locus on chromosome 13q12 comprising a FLAP nucleic acid, wherein the presence of the haplotype is diagnostic of a susceptibility to myocardial infarction or stroke.

41. A method of diagnosing a susceptibility to myocardial infarction or stroke in an individual, comprising determining the presence or absence in the individual of a haplotype selected from the group consisting of: haplotypes shown in Table 4, wherein the presence of the haplotype is diagnostic of a susceptibility to myocardial infarction or stroke.

42. A method of diagnosing a susceptibility to myocardial infarction or stroke in an individual, comprising determining the presence or absence in the individual of a haplotype selected from the group consisting of: haplotypes shown in Table 5, wherein the presence of the haplotype is diagnostic of a susceptibility to myocardial infarction or stroke.

43. A method of diagnosing a susceptibility to myocardial infarction or stroke in an individual, comprising determining the presence or absence in the individual of a haplotype selected from the group consisting of: haplotypes shown in Table 13, wherein the presence of the haplotype is diagnostic of a susceptibility to myocardial infarction or stroke.

44. A method of diagnosing a susceptibility to myocardial infarction or stroke in an individual, comprising determining the presence or absence in the individual of a haplotype selected from the group consisting of: haplotype B4,

B5, B6, A4 and A5, wherein the presence of the haplotype is diagnostic of a susceptibility to myocardial infarction or stroke.

45. A method of diagnosing a susceptibility to myocardial infarction or stroke in an individual, comprising determining the presence or absence in the individual of a haplotype HapB, wherein the presence of the haplotype is diagnostic of a susceptibility to myocardial infarction or stroke.

46. A method for the diagnosis of increased risk of susceptibility to myocardial infarction or stroke in an individual, comprising: screening for an at-risk haplotype in the FLAP nucleic acid that is more frequently present in an individual susceptible to myocardial infarction or stroke compared to an individual who is not susceptible to myocardial infarction or stroke wherein the at-risk haplotype increases the risk significantly.

47. The method of Claim 46, wherein the significant increase is at least about 20%.

48. The method of Claim 46, wherein the significant increase is identified as an odds ratio of at least about 1.2.

49. A method for the diagnosis of increased risk of susceptibility to myocardial infarction or stroke in an individual, comprising: screening for an at-risk haplotype in the FLAP nucleic acid that is more frequently present in an individual susceptible to myocardial infarction or stroke (affected), compared to the frequency of its presence in a healthy individual (control), wherein the presence of the at-risk haplotype is indicative of a susceptibility to myocardial infarction or stroke.

50. The method of Claim 49, wherein screening for the presence of an at-risk haplotype comprises screening for an at-risk haplotype within or near FLAP

that significantly correlates with a haplotype selected from the group consisting of: a halotype shown in Table 4; a haplotype shown in Table 5; a haplotype shown in Table 13; haplotype B4; haplotype B5; haplotype B6; haplotype A4; haplotype A5; and haplotype HapB.

51. The method of Claim 49, wherein screening for the presence of an at-risk haplotype comprises screening for an at-risk haplotype within or near FLAP that significantly correlates with susceptibility to myocardial infarction or stroke.

52. A method for the diagnosis of increased risk of susceptibility to myocardial infarction or stroke in an individual, comprising: screening for an at-risk haplotype in the FLAP nucleic acid that is more frequently present in an individual susceptible to myocardial infarction or stroke (affected), compared to the frequency of its presence in a healthy individual (control), wherein the haplotype has a p value of < 0.05, and wherein the presence of the haplotype is diagnostic of a susceptibility to myocardial infarction or stroke.

53. The method of Claim 52, wherein the at-risk haplotype comprises one or more markers set forth in Table 3.

54. A method of diagnosing FLAP-associated myocardial infarction or stroke in an individual who has had a myocardial infarction and/or a stroke, comprising detecting a polymorphism in a FLAP nucleic acid, wherein the presence of the polymorphism in the nucleic acid is indicative of FLAP-associated myocardial infarction or stroke.

55. A method of diagnosing FLAP-associated myocardial infarction or stroke in an individual who has had a myocardial infarction and/or a stroke, comprising detecting an alteration in the expression or composition of a polypeptide encoded by a FLAP nucleic acid in a test sample, in comparison with the

expression or composition of a polypeptide encoded by a FLAP nucleic acid in a control sample, wherein the presence of an alteration in expression or composition of the polypeptide in the test sample is indicative of FLAP-associated myocardial infarction or stroke.

56. . A method of diagnosing FLAP-associated myocardial infarction or stroke in an individual who has had a myocardial infarction and/or a stroke, comprising determining the presence or absence in the individual of a haplotype selected from the group consisting of: haplotypes shown in Table 4, wherein the presence of the haplotype is diagnostic of FLAP-associated myocardial infarction or stroke.

57. A method of diagnosing FLAP-associated myocardial infarction or stroke in an individual who has had a myocardial infarction and/or a stroke, comprising determining the presence or absence in the individual of a haplotype selected from the group consisting of: haplotypes shown in Table 5, wherein the presence of the haplotype is diagnostic of FLAP-associated myocardial infarction or stroke.

58. A method of diagnosing FLAP-associated myocardial infarction or stroke in an individual who has had a myocardial infarction and/or a stroke, comprising determining the presence or absence in the individual of a haplotype selected from the group consisting of: haplotypes shown in Table 13, wherein the presence of the haplotype is diagnostic of FLAP-associated myocardial infarction or stroke.

59. A method of diagnosing FLAP-associated myocardial infarction or stroke in an individual who has had a myocardial infarction and/or a stroke, comprising determining the presence or absence in the individual of a haplotype selected from the group consisting of: haplotype B4, B5, B6, A4 and A5, wherein the

presence of the haplotype is diagnostic of FLAP-associated myocardial infarction or stroke.

60. A method of diagnosing FLAP-associated myocardial infarction or stroke in an individual who has had a myocardial infarction and/or a stroke, comprising determining the presence or absence in the individual of a haplotype HapB, wherein the presence of the haplotype is diagnostic of FLAP-associated myocardial infarction or stroke.